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The Dutch Lung Cancer Audit: Nationwide quality of care evaluation of lung cancer patients

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ABSTRACT

Objectives: This study describes the initiation of the Dutch Lung Cancer Audit for Lung Oncology (DLCA-L) and reports the first results of three years of clinical auditing.
Methods: The initiation, dataset, and data quality of the DLCA-L are described. For the analyses, all patients registered from 2017 to 2019 were included. Descriptive statistics were used to assess the first outcomes of the DLCA-L, including results from quality indicators, patient- and tumor characteristics, and the real-world use of immunotherapy.
Results: The DLCA-L was initiated after the surgery and radiotherapy audit for lung cancer. In total, 33.788 NSCLC patients and 4.293 SCLC patients were registered in the DLCA-L from 2017 to 2019. Seventy-three (97 %) Dutch hospitals participated in the DLCA-L in 2019. The registry became nation-wide in 2020. The data quality improved over the years, with complete cases in 90 % of the NSCLC patients. In total, 15 quality indicators were established based on DLCA-L data to improve processes and clinical outcomes. An example of these quality indicators was brain imaging at diagnosis of stage III NSCLC patients, which increased from 80 % in 2017 to 90 % in 2019 and hospital variation was reduced. The DLCA-L provided data on immunotherapy use in stage IV NSCLC ($n = 4.415$) patients. These patients had a median age of 67 years and 11 % of the patients had an ECOG PS ≥ 2. The number of patients treated with immunotherapy in different hospitals varied between 2 patients to 163 patients per hospital.
Conclusion: The DLCA-L has become a valuable and complete data source with national coverage in 2020. A high number of registered patients and limited missing data resulted in better insights into hospital processes and outcomes of lung cancer care. Quality indicators were, with success, used to establish improvements and minimize hospital variation. The DLCA-L also provides hospitals real-world information on the use of (systemic) therapies.

Abbreviations: CI, confidence intervals; DCRA, Dutch Colorectal Audit; DICA, Dutch Institute for Clinical Auditing; DLCA-L, Dutch Lung Cancer Audit for Lung Oncology; DLCA-R, Dutch Lung Cancer Audit for Radiotherapy; DLCA-S, Dutch Lung Cancer Audit for Surgical treatment; DLCR, Danish Lung Cancer Registry; ECOG PS, Eastern Cooperative Oncology Group Performance Score; ICHOM, International Consortium for Healthcare Outcomes Measurement; MRDM, Medical Research Data Management; NCR, Netherlands Cancer Registry; NLCA, National lung cancer audit (United Kingdom); NLCR, National Quality Registry for Lung Cancer (Sweden); NSCLC, non-small cell lung cancer; NVALT, Dutch professional association of chest physicians; OS, overall survival; PFS, progression-free survival; SCLC, small-cell lung cancer; SONCOS, The Dutch Federation of Oncologic Societies; ZiN, Dutch healthcare institute; ZN, umbrella organization of healthcare insurers in the Netherlands.

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1. Introduction

Clinical auditing proved to be a valuable process for the improvement of medical care and patient outcomes [1]. The use of quality registries or clinical audits has been effective in the last decade in evaluating and improving medical care by minimizing undesired practice variation and improving patient outcomes. National audits for lung cancer patients included mostly surgical treatment of lung cancer [2–4].

Nationwide lung cancer registries, such as the National Lung Cancer Audit (NLCA), showed in 2017 practice variation in the number of stage III and IV non-small cell lung cancer (NSCLC) patients treated with anticancer systemic therapy and a difference in 1-year survival across organizations [5]. Registries provide data on hospital variation and improvements of care but are also valuable in generating real-world data, leading to a better understanding of daily clinical practice [6].

Registries are also valuable in the evaluation of medicines after marketing authorization by measuring real-world effectiveness and long-term safety. Immunotherapy treatment, for example, gained interest in stage III and stage IV NSCLC patients when trials showed significant improvements in progression-free survival (PFS) and overall survival (OS) [7–10]. Real-world data research in immunotherapy treated NSCLC patients showed an efficacy-effectiveness gap of 25 %, resulting in poorer outcomes for real-world treated patients [11]. Registries can provide real-world effectiveness data on these medicines on a nation-wide level. Immunotherapy treatment results from a real-world setting were provided by the National Immunotherapy Registry, including lung cancer patients from 2015 to 2017 in the Netherlands [12].

In 2012, the Dutch Lung Cancer Audit for Surgical treatment (DLCA-S) was initiated, which became a mandatory registry in 2015, leading to a nationwide population-based registry in the Netherlands [13]. The DLCA-S does not include radiotherapy and systemic treatment of lung cancer patients.

The Dutch Lung Cancer Audit for Lung Oncology (DLCA-L) was set up in 2015 to provide insights into the quality of care of lung cancer patients treated with systemic therapy by focusing on diagnostics, monitoring of in-hospital times and outcomes of systemic therapy. The professional association of chest physicians (NVALT) made participation in the DLCA-L mandatory. The DLCA-L provides feedback information to hospitals to stimulate the improvement of clinical care for lung cancer patients. Registered data of the hospitals are analyzed, and benchmarked indicator results on the quality of their care processes and patient outcomes are fed back in secured web-based dashboards to the hospitals [14].

This study describes the initiation of the DLCA-L and reports the first results of three years of clinical auditing.

2. Methods

2.1. Organizational structure

In 2015, the DLCA-L was initiated by the professional association of chest physicians (NVALT). The registry is facilitated by the Dutch Institute for Clinical Auditing (DICA), a non-profit organization, which is structurally funded by the umbrella organization of healthcare insurers in the Netherlands (ZN) [15]. DICA facilitates 22 nation-wide quality registries [16]. The DLCA-L is part of the multidisciplinary Dutch Lung Cancer Audit (DLCA), which consists of three clinical audits: DLCA-Surgery (DLCA-S), DLCA-Radiotherapy (DLCA-R), and the sub-registry for the diagnosis and systemic treatment of lung cancer (DLCA-L). A clinical audit board, consisting of medical specialists mandated by their professional association, leads the DLCA. Every sub-registry has a scientific committee with experts from the field. The scientific committee of the DLCA-L, consisting of pulmonologists, gathers four times a year to discuss results from the DLCA-L, develop new quality indicators, and improve the dataset. The three sub-registries of the DLCA are not merged yet due to privacy legislation. The separate data sources will be linked in the future to improve data on the total treatment of lung cancer patients. The sub-registries work together in projects, developing quality indicators and improving the registries.

2.2. Database

Data collection in the DLCA-L started in January 2015, including all patients diagnosed with (clinically suspected) primary lung carcinoma. In the registry, the suspected indication is further specified with data on pathological confirmation when present. Carcinoma in situ and invasive tumors are included. Premalignant disorders are excluded. Patients under 18 are not registered in the DLCA-L. The database consists of patient identifiers, the episode, and the follow-up. In the episode, detailed clinical information on baseline patient- and tumor characteristics, diagnostics, and first-line treatment are registered. Toxicity is scored using the CTC AE criteria. The options for toxicity after treatment (different modules for chemotherapy, immunotherapy and targeted therapy) are: “No toxicity or toxicity with grade <3″ or “Toxicity with grade ≥ 3. Another important variable in the episode section is the treatment intention of lung cancer patients. Curative treatment intention is defined as the treatment of patients with the intent to cure them instead of reducing symptoms. Every non-curative treatment defines palliative treatment intention. The mandatory 1-year follow-up section consists of information on treatment response, follow-up treatments, and the date and cause of death. These data can be used to calculate 1-year PFS and OS. The database contains 153 variables, of which 44 % is mandatory and should be registered by all hospitals to analyze the data for quality indicators (**Supplement 1**). The total list of variables used in the DLCA-L is freely accessible at the DICA website [17].

In 2020, the DLCA-L dataset was expanded with variables from the NVALT “National Immunotherapy Registry” [12]. This registry was initially a separate nation-wide registry focusing on immunotherapy treatment, including PD-L1 expression and the different lines of therapy patients received. Registration also included information on safety and hospital admission rate and duration [12]. The NVALT registry was merged with the DLCA-L to reduce the registration burden as a result of multiple lung cancer registries. A summary of the DLCA-L dataset is shown in **Supplement 1**.

In compliance with Dutch regulations, no patient informed consent or approval of the medical ethical committee was necessary for registration in the DLCA-L. Data from the hospitals is processed by Medical Research Data Management (MRDM). Privacy issues and informed consent of patients is established in the contracts between the hospitals and MRDM. For the initiation of the DLCA-L, no other privacy issues were necessary other than already consisting of contracts between DICA and MRDM involving the processes with anonymized data.

2.3. Data quality and validation

The data quality of the DLCA-L is assured by using precise definitions for the variables in the registry, described in a manual for data managers. Data managers are often quality employees in hospitals and commonly trained and qualified to register quality registry data. The web-based data-collection environment also includes technical conditions and validations for specific data entry items to minimize unreliable data. Patient records with missing data of required variables are notified on a digital signal list and the record cannot be completed if mandatory data are missing. Involved medical specialists supervise entered data. Data validation is realized by independent external reviewers comparing registered DLCA-L data records with data in the electronic patient records of the hospital.

2.4. Quality indicators

Quality indicators are established by the scientific committee and

external parties, such as ZN and the Dutch Health Care Institute (ZiN). Quality indicators are based on national quality standards and evidence-based guidelines. In the Netherlands, quality is assured by using the SONCOS (the Dutch Federation of Oncologic Societies) quality standards. Specific thresholds for quality indicators are therefore not mentioned by the DLCA-L. One of the requirements mentioned in SONCOS is participation in the DLCA-L. The SONCOS requirements are used in the DLCA-L to set up the registry and to develop new quality indicators, i.e., brain imaging in stage III NSCLC patients. Since 2015, DLCA-L data led to the development of 15 quality indicators. Quality indicator results lead to information on the quality of care of individual hospitals, which are analyzed and discussed by the professional association. Hospitals receive their data compared to the benchmark, visualized in funnel plots, to improve processes in hospitals. Hospital specific results of a selected set of indicators are shared with stakeholders and are publicly available.

2.5. Statistical analysis

The first outcomes of the DLCA-L were assessed using descriptive statistics. Outcomes included patient-, tumor-, and treatment characteristics of NSCLC and small-cell lung cancer (SCLC) patients, diagnosed and registered from 2017 to 2019. Descriptive statistics were also used to analyze complete cases and the use of immunotherapy in a real-world setting. Complete cases were defined as no missing data in all of the following essential variables in the registry: date of birth, gender, subgroup disease, date of the first hospital visit, Eastern Cooperative Oncology Group Performance Score (ECOG PS) and molecular diagnosis.

The results of the 15 quality indicators are presented for 2017 until 2019, including the variation (minimum and maximum outcomes) between hospitals. Quality indicator results are presented to the hospitals in funnel plots using 95 % and 99 % CI limits [18]. In a funnel plot, the observed rate of a specific indicator is plotted against the volume of the hospital. The 95 % and 99 % CI limits change in relation to the number of patients per hospital [18,19]. Variation in brain imaging among individual hospitals was visualized in a funnel plot as an example.

Data handling and statistical analyses were performed using the R software system for statistical computing (version 3.6.1.; packages tidyr, lubridate, tableone, ggplot2, ggthemes, dplyr, ggpubr, RColorBrewer).

3. Results

3.1. Patient population

The total number of diagnosed lung cancer patients in three years (2017–2019) registered in the DLCA-L consisted of 33.788 NSCLC patients and 4.293 SCLC patients. The number of hospitals that participated in the DLCA-L has changed over the years, from 39 (2015), 73 (2016), 74 (2017), 75 (2018) to 73 hospitals in 2019. Of all Dutch hospitals treating lung cancer, 97 % participated in the DLCA-L in 2019. The number of diagnosed lung cancer patients per hospital varied between 3 and 496 patients, with an average of 181 patients per hospital (**Supplement 2**). All Dutch hospitals are participating in the DLCA-L in 2020.

The total number of NSCLC patients registered in the DLCA-L has increased from 10.061 patients in 2017, 11.904 patients in 2018, to 11.823 patients in 2019. The number of registered SCLC patients stayed constant over time. The Netherlands Cancer Registry has reported an incidence of over 13.000 lung cancer patients a year since 2017 [20]. In **Supplement 3**, the proportions of patients in which the registration is complete (complete cases) are shown. Complete cases for NSCLC patients were 88 % (2017), 87 % (2018) and 90 % (2019). The proportion of complete cases in SCLC patients in 2019 was 89 % (**Supplement 3**).

Patient- and treatment characteristics of registered NSCLC and SCLC patients are shown in Table 1. The proportion of not available or unknown information of the mandatory variables was ≤10 %. In the NSCLC patient group, 56 % was male and 44 % female, the median age was 70 years, and 31 % of the patients were older than 75 years. Of these real-world patients, 22 % had an ECOG PS ≥ 2.

Table 1
Patient- and tumor characteristics of all NSCLC and SCLC patients registered in the DLCA-L from 2017 to 2019.

		NSCLC	SCLC
n		33.788	4.293
Year of first hospital visit; n(%)	2017	10.061 (30)	1.401 (33)
	2018	11.904 (35)	1.472 (34)
	2019	11.823 (35)	1.420 (33)
Age; median (range)		70 (18, 101)	69 (24, 117)
Age; n(%)	<65	10.439 (31)	1.419 (33)
	65–75	12.839 (38)	1.771 (41)
	>75	10.510 (31)	1.103 (26)
Gender; n(%)	Male	18.741 (56)	2.124 (50)
	Female	15.018 (44)	2.165 (50)
	Unknown	29 (0)	4 (0)
Stage; n(%)	0	306 (1)	17 (0)
	I	6793 (20)	102 (2)
	II	2801 (8)	119 (3)
	III	6.524 (19)	989 (23)
	IV	15.156 (45)	2.850 (66)
	Unknown	2.208 (7)	216 (5)
ECOG PS; n(%)	≤1	23.024 (68)	2.741 (64)
	≥2	7.516 (22)	1.143 (27)
	Unknown	3.248 (10)	409 (10)
Diagnosis; n(%)	Cytology	6.670 (20)	1.210 (28)
	Histology	14.591 (43)	2.133 (50)
	Only imaging	4.550 (14)	91 (2)
	Resection-histology	994 (3)	15 (0)
	Unknown	6.983 (21)	844 (20)
Treatment intention*; n(%)	Curative	14.861 (44)	1.045 (25)
	Palliative	17.321 (51)	3.100 (72)
	Unknown	1.606 (5)	148 (3)

ECOG PS = Eastern Cooperative Oncology Group Performance Score
NSCLC = Non-small-cell lung cancer.
SCLC = Small-cell lung cancer.
* Curative treatment intention refers to the treatment of patients with the intent to cure them instead of reducing symptoms. Every non-curative treatment defines palliative treatment intention.

3.2. Quality indicators

The 15 quality indicators are described in Table 2, with average outcome and variation between hospitals from 2017 to 2019. The definitions of the quality indicators can be found in **Supplement 4**. The quality indicators showed improvements in registration completeness and diagnostic processes over the years. Data completeness improved from 88 % (2017) to 93 % (2019). An increase of 89 % (2017) to 93 % (2019) in the performance of molecular diagnostics in stage IV adenocarcinoma patients was reached. Toxicity after chemotherapy treatment in stage IV NSCLC patients <70 years showed a decrease of 19 % (2017) to 12 % (2019). An example of how hospitals receive their data compared to the benchmark in a funnel plot is shown in Fig. 1. This funnel plot shows the variation in brain imaging in stage III NSCLC patients among hospitals, which varied between 25−100% in 2017 (Fig. 1a). Hospital variation was reduced in 2019 (56−100%), and the overall performance of all hospitals increased from 80 % in 2017 to 90 % in 2019 (Fig. 1b).

3.3. First-line treatment choices

Fig. 2 shows first-line treatment choices of all NSCLC patients treated with active tumor treatment (with curative or palliative intention) in the Netherlands between 2017 and 2019. Registration of patients that

Table 2
Structure-, process, and outcome quality indicators of the DLCA-L.

Indicator type and number	Description	2017	2018	2019
Structure				
1.	Complete registration of registered lung cancer patients in the DLCA-L; %	88 (0–100)	90 (29–100)	93 (60–100)
2.	Newly diagnosed primary lung cancer patients registered in the DLCA-L; n	10.545	12.504	12.562
3.	Hospitals treating more than 50 lung cancer patients per year; %	93	93	97
Process				
4.	Stage III NSCLC patients undergoing brain imaging before the start of systemic therapy with curative intention; %	82 (25–100)	83 (25–100)	90 (56–100)
5.	Stage IV adenocarcinoma lung cancer patients undergoing molecular diagnostics before the start of systemic therapy with curative intention; %	89 (50–100)	92 (59–100)	93 (71–100)
6.	Patients discussed in multidisciplinary consultation before treatment; %			
	a.Stage I-III curative treatment	98 (82–100)	99 (67–100)	99 (80–100)
	b.Palliative treatment	98 (73–100)	98 (62–100)	98 (66–100)
7.	Duration of diagnostic trajectory; %			
	a. < 21 days without invasive mediastinal diagnostics	62 (30–100)	60 (0–100)	62 (0–100)
	b. < 21 with EUS/EBUS, but without mediastinoscopy	44 (0–100)	44 (0–80)	46 (0–100)
	c. < 35 days with mediastinoscopy	54 (0–100)	53 (0–100)	59 (0–100)
8.	Diagnostics of stage III NSCLC patients with EUS/EBUS; %	59 (7–100)	56 (0–100)	61 (0–100)
9.	Stage III NSCLC patients treated with adjuvant chemotherapy; %	12 (0–67)	15 (0–100)	15 (0–100)
10.	First-line systemic treatment of stage IV NSCLC patients without curative intention; %			
	a. Chemotherapy	31 (0–85)	25 (0–47)	30 (0–60)
	b. Immunotherapy	8 (0–46)	18 (0–61)	33 (0–67)
	c. Targeted therapy	6 (0–39)	8 (0–32)	10 (0–100)
11.	First-line systemic treatment of stage IV SCLC patients without curative intention; %			
	a. Chemotherapy	65 (0–100)	64 (0–100)	68 (0–100)
	b.Immunotherapy	0 (0–13)	2 (0–29)	5 (0–74)
12.	Use of immunotherapy in elderly patients with stage IV NSCLC disease with no curative intention; %			
	a. < 70 years	8 (0–43)	18 (0–59)	35 (0–73)
	b. > 70 years	5 (0–49)	14 (0–62)	23 (0–59)
13.	Use of chemo-immunotherapy in elderly patients with stage IV NSCLC disease with no curative intention; %			
	a. < 70 years	1 (0–10)	4 (0–27)	23 (0–64)
	b. > 70 years	0 (0–11)	2 (0–15)	13 (0–40)
Outcome				
14.	Toxicity after treatment with systemic therapy in stage IV NSCLC young (<70 years) patients; %			
	a. Chemotherapy	19 (0–100)	13 (0–60)	12 (0–100)
	b. Immunotherapy	7 (0–50)	5 (0–50)	7 (0–73)
	c. Targeted therapy	7 (0–100)	8 (0–100)	8 (0–100)
	d. Chemo radiotherapy	14 (0–100)	13 (0–100)	5 (0–100)
15.	Toxicity after treatment with systemic therapy in stage IV NSCLC elderly (>70 years) patients; %			
	a. Chemotherapy	19 (0–56)	18 (0–100)	11 (0–55)
	b.Immunotherapy	6 (0–100)	7 (0–100)	6 (0–56)
	c.Targeted therapy	11 (0–100)	12 (0–100)	10 (0–100)
	d.Chemo radiotherapy	27 (0–100)	8 (0–100)	2 (0–33)

The outcomes of the quality indicators are presented on a nation-wide level with an average of the outcomes of all hospitals and the minimum and maximum outcome of all hospitals from 2017 to 2019. More information on the definitions of the quality indicators can be found in supplement 4.

receive best supportive care is not further specified. The most used treatments in stage 0-II NSCLC patients were radiotherapy and surgery. This did not differ over the years 2017 to 2019. Radiotherapy treatment was used in 42 % of the patients in 2017, 44 % in 2018, and 43 % in 2019. Of all stage 0-II NSCLC patients, 42 % received surgery in 2017, 43 % in 2018, and 46 % in 2019. In stage III NSCLC patients, 39 % received chemo-radiotherapy in 2019. In stage IV patients, the increase in immunotherapy led to a decrease in chemotherapy treatment. The number of unknown treatments has drastically decreased to 0% between 2017 and 2019.

3.4. Increase in immunotherapy use

Since 2016, multiple immunotherapies became available in the Netherlands (nivolumab in March 2016, pembrolizumab in July 2017, durvalumab in June 2018, and atezolizumab in September 2019) after receiving marketing authorization by the European Medicines Agency (EMA) for treatment of locally advanced and metastatic NSCLC. The percentage of stage III and stage IV NSCLC patients treated with immunotherapy or immune-chemotherapy increased over the years. Immunotherapy treatment consisted of 15 % of all treatments in 2017, followed by 33 % in 2018 and 57 % in 2019. Stage III NSCLC patients received relatively less immunotherapy treatment, 3.5 % in 2017, 13 % in 2018, and 25 % in 2019. Durvalumab has been indicated for stage III NSCLC patients who have been treated with previous concurrent chemoradiotherapy.

Patient- and tumor characteristics of immunotherapy treated patients (n = 4,415) from 2017 to 2019 are shown in Table 3. Although phase-III trials included relatively young and fit patients, in real-world

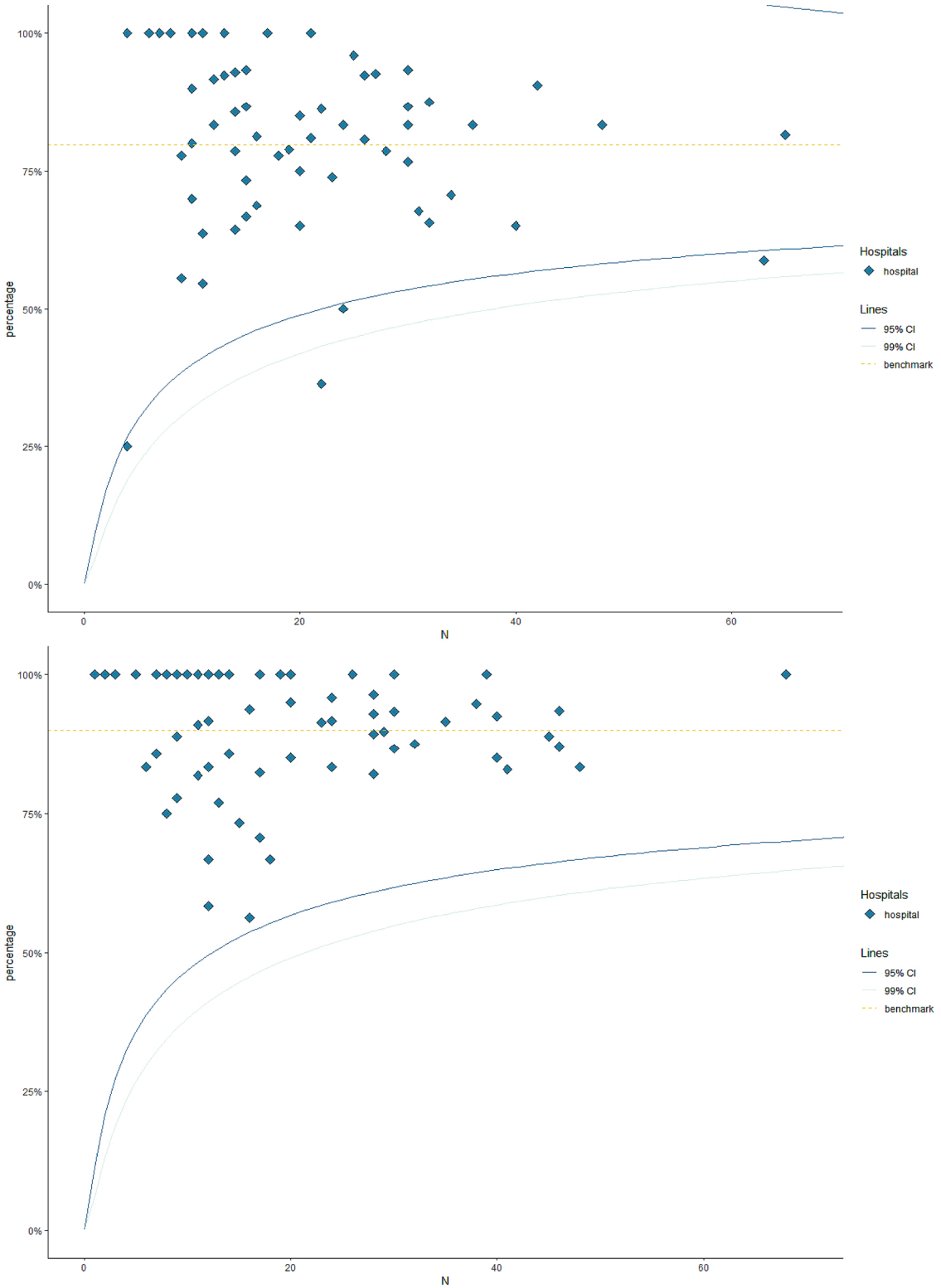

Fig. 1. Percentage of stage III NSCLC patients registered in the DLCA-L undergoing brain imaging with PET or CT before the start of therapy with curative intention in 2017 (upper graph, 1a) and 2019 (lower graph, 1b). Every symbol is a hospital in the Netherlands. The x-axis shows the number of stage III NSCLC patients receiving therapy per hospital.

practice, the median age was 67 years, 17 % was older than 75 years, and 11 % of the patients had an ECOG PS of ≥2. In 2019, 75 % of the patients underwent molecular diagnostics, including PD-L1 expression and mutation analyses (KRAS/EGFR/ALK/EML-4-ALK) (Table 3).

Immunotherapy use in elderly (75–80 years) was 36 % and similar to the use in patients of 70–75 years, which was 38 %. Thirty percent of the patients older than 80 years (n = 689) were treated with immunotherapy. Of all patients >80 years, 23 % had an ECOG PS ≥ 2, compared to 17 % in patients aged 70–75 years. The percentage of ECOG PS ≥ 2 increased with increasing age. The use of immunotherapy among stage

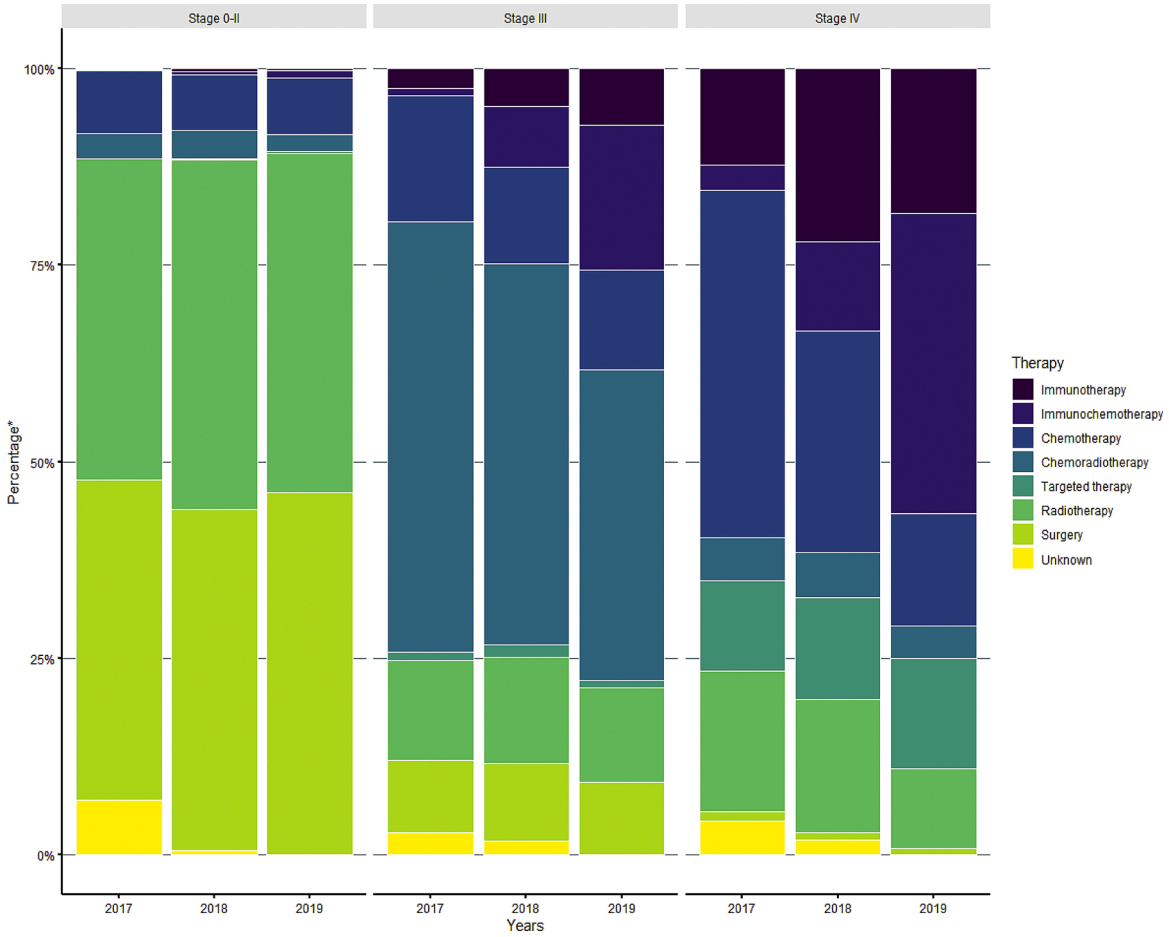

Fig. 2. First-line treatment (combinations) of NSCLC patients with active tumor treatment (surgery and radiotherapy with curative intention or/and (palliative) chemotherapy, immunotherapy, or targeted therapy) from 2017 to 2019.

IV NSCLC patients with different age categories is shown in **Supplement 5**.

Immunotherapy treatment was not immediately available in all hospitals in the Netherlands. In the early years, patients were referred to specialized hospitals to receive immunotherapy treatment. In 2017, 60 hospitals treated patients with immunotherapy, but this number of hospitals increased over the years to 72 hospitals in 2019. In 2017, only 5 of 60 hospitals treated more than 20 patients with immunotherapy. In 2019 the number of patients treated with immunotherapy varied between hospitals from 2 patients to 163 patients (Fig. 3).

In total, three dynamic web-based dashboards have been developed for the DLCA-L. The quality indicators are presented in counts and funnel plots in Codman Indicators. The patient population and the outcomes and trends are presented in Codman Exploration, in which filters can be used to select specific patient-, tumor- and treatment characteristics. Outcomes and trends can be compared to the benchmark. The third dashboard is Codman Descriptives, which includes basic information on the patients registered in the own hospital compared to the benchmark. Examples of the dashboards can be found in **Supplement 6**.

4. Discussion

Within three years, the DLCA-L has become a valuable registry for clinical auditing of systemically treated lung cancer patients in the Netherlands. By improving data completeness, nationwide hospital participation, and the development of valuable quality indicators, the DLCA-L gave insight into the real-world treatment landscape of lung cancer patients and the variation in processes between hospitals.

4.1. Comparison with other audits

The completeness of the DLCA-L dataset improved over the years and is considered a reliable data source since 2017 since the number of registered lung cancer patients equals the lung cancer incidence of the Netherlands Cancer Registry (NCR) [20]. Compared to the NCR, the DLCA-L data consisted of 82 % (2017), 97 % (2018), and 96 % (2019) of the NCR published incidence. A small number of patients has not been registered in the DLCA-L when treatment consisted only of surgery. However, these patients are registered in the surgical audit, DLCA-S. The relatively high numbers of registered patients are considered as a reliable, population-based representation of all lung cancer patients in the Netherlands. The number of hospitals participating in the DLCA-L decreased from 2018 to 2019, which can be explained by the fact that hospitals merged over time.

The Danish Lung Cancer Registry (DLCR) was established in 2000, and data completeness was considered sufficient from 2003 [21]. The DLCR also created quality indicators to improve lung cancer care, mainly focusing on the surgical treatment of lung cancer patients. A study from 2013 reported outcomes of the quality indicators from the DLCR, including a structural quality indicator measuring the waiting time after referral (<42 days). This quality indicator cannot be compared to the quality indicator of the DLCA-L, since the time from the first visit in the hospital to the first oncological treatment is measured in the Netherlands instead of the first referral [21]. The incidence of lung cancer in Denmark is significantly lower than in the Netherlands. The

Table 3
Patient- and tumor characteristics of first-line immunotherapy treated patients.

		2017	2018	2019
Patients; n		486	1.375	2.554
Age; median (range)		67 (31, 88)	66 (24, 117)	67 (24, 90)
Age; n(%)	<65	205 (42)	607 (44)	1.080 (42)
	65−75	202 (42)	526 (38)	1.034 (41)
	>75	79 (16)	242 (18)	440 (17)
Gender; n (%)	Male	257 (53)	725 (53)	1.429 (56)
	Female	227 (47)	650 (47)	1.123 (44)
	Unknown	2 (0)	0	2 (0)
Subgroup; n(%)	NSCLC	479 (99)	1.352 (98)	2.490 (98)
	SCLC	7 (1)	23 (2)	64 (2)
Stage; n(%)	0-II	7 (1)	22 (2)	40 (2)
	III	54 (11)	228 (17)	459 (18)
	IV	362 (75)	1.065 (78)	1.962 (77)
	Unknown	63 (13)	60 (4)	93 (4)
ECOG PS; n(%)	<2	388 (80)	1.125 (82)	2.149 (84)
	≥2	67 (14)	147 (11)	276 (11)
	Unknown	31 (6)	103 (8)	129 (5)
Molecular diagnostics; n(%)	No	91 (19)	256 (19)	543 (21)
	Yes	362 (74)	1.051 (76)	1.925 (75)
	Yes, but not successful	5 (1)	9 (1)	26 (1)
	Unknown	28 (6)	59 (4)	60 (2)
Treatment intention; n(%)	Curative intention	94 (19)	242 (18)	463 (18)
	Palliative	326 (67)	1.071 (78)	2.061 (81)
	Unknown	66 (14)	62 (5)	30 (1)

ECOG PS = Eastern Cooperative Oncology Group Performance Score.
NSCLC = Non-small-cell lung cancer.
SCLC = Small-cell lung cancer.

DLCR reported almost 39.000 registered patients from 2003 to 2012, while the DLCA-L has over 43.000 records registered from 2017 to 2019. The population of Denmark is 5.7 million (2019) compared to 17.3 million (2019) in the Netherlands [22,23].

The incidence of lung cancer registered in the Swedish National Quality Registry for Lung Cancer (NLCR) is around 3000 patients a year, compared to 13.000 patients newly diagnosed lung cancer patients in the Netherlands. Patient coverage in the NLCR was 94 % in 2014, which is comparable with the DLCA-L [24]. As to our knowledge, outcomes of lung cancer quality indicators from the NLCR are not reported.

Compared to the NLCA of the UK, the DLCA-L is a starting audit. This results in different outcome measurements between the two audits. While data from the NLCA is sufficient enough to measure survival outcomes, the DLCA-L has been primarily focusing on data quality, data completeness and intern processes [25]. The NLCA reported 83 % of advanced adenocarcinoma patients underwent molecular testing in 2017. The DLCA-L reported a score of 89 %, but differences in definitions of these quality indicators made it impossible to compare outcomes. While the NLCA specifies molecular testing as testing of three biomarkers (EGFR, ALK and PD-L1), the definition of the DLCA-L quality indicator does not include the type of molecular testing [26]. Linkage of the DLCA-L to insurers data on death will lead to the establishment of survival data. The NLCA reported over 39.000 diagnosed patients in 2017, which is three times the lung cancer incidence numbers in the Netherlands. In examining the total amount of newly diagnosed Lung cancer patients it is important not only to include pathologically confirmed cases, but also unconfirmed cases to get an complete overview.

4.2. Outcomes

An important purpose of continuous feedback to medical specialists on the DLCA-L quality indicators is the improvement of in-hospital processes and guideline adherence. Quality indicators may show hospital variation, and therefore improvements in care can be made, resulting in fewer hospital outliers and more similar outcomes. Information on hospital outliers is notified to the professional association, which is in the lead to discuss these quality issues with their colleagues in the underperforming hospital to improve on certain processes or outcomes. In the DLCA-L, hospitals have been anonymized until recently, since it was a starting registration. Though professional associations of other quality registries facilitated by DICA, such as the Dutch Colorectal Audit (DCRA), receive hospital-specific data from the registry and discuss these with the participating hospitals to improve care on a local level. The Association of Surgeons in the Netherlands, for example, made participation in the DCRA mandatory and also agreed with their members in their General Assembly that hospital-specific data are available for the board and can be used in visitations to hospitals. Data are also used to evaluate the adherence to the quality standards established by the same societies. The scientific committee of the DLCA-L evaluates the improvements in quality indicators and adjust and improve these when needed.

A first example of outcomes from the DLCA-L showed that brain imaging at diagnosis in stage III NSCLC patients, who are candidates for combined modality treatment, was not standard care in specific hospitals, despite the recommendations in national and international guidelines [27,28]. The funnel plot was used to assess the variation between hospitals, taking into account random variability. In 2017, four hospitals were considered as outliers. With the benchmark information, these hospitals got insights into their procedures, leading to an improvement in adherence to guidelines. The average percentage of patients undergoing brain imaging increased and the variation between hospitals decreased from 2017 to 2019. However, the outcomes of other quality indicators showed that there is still room for improvement. The duration of the diagnostic trajectory, for example, is still not within the range agreed on in quality standards for each patient. The improvement in data completeness of the DLCA-L over the years results in more trustworthy outcomes for the quality indicators. Differences in the more recently established quality indicators (10−15) can also be partly explained by improvements in the registration of variables necessary for these indicators. Stimulating improvement is in line with the primary purpose of the DLCA-L: quality assurance of the diagnostics of lung cancer patients, the in-hospital processes, and the treatment with systemic therapies. Continuous feedback and the possibility to explore the data to individual patient level in the Codman dashboards, called after the founder of clinical auditing, made improvement cycles less time-consuming [16].

Outcomes from the DLCA-L can also be used to receive insights in real-world clinical practice. Treatment with immunotherapies gained significant interest in past years, and significantly higher use of immunotherapy was seen. Real-world NSCLC patient characteristics treated with immunotherapy differed from patients included in clinical studies. These trials excluded patients with ECOG PS ≥ 2, while 11 % of the real-world patients had this characteristic. The phase III trials researching immunotherapies (KEYNOTE-024, CheckMate-057, OAK, and PACIFIC) included in general more male patients, while this is almost equal for real-world treated patients [7–10]. Treated real-world patients were older than included trial patients. These differences between trial and real-world patients also occur in advanced melanoma patients. Clinical outcomes (OS, PFS) of treated real-world patients could, therefore, be poorer than in trials. The accurate and complete registration of survival in the DLCA-L has been one of the main goals for improvement and will be available in the near future.

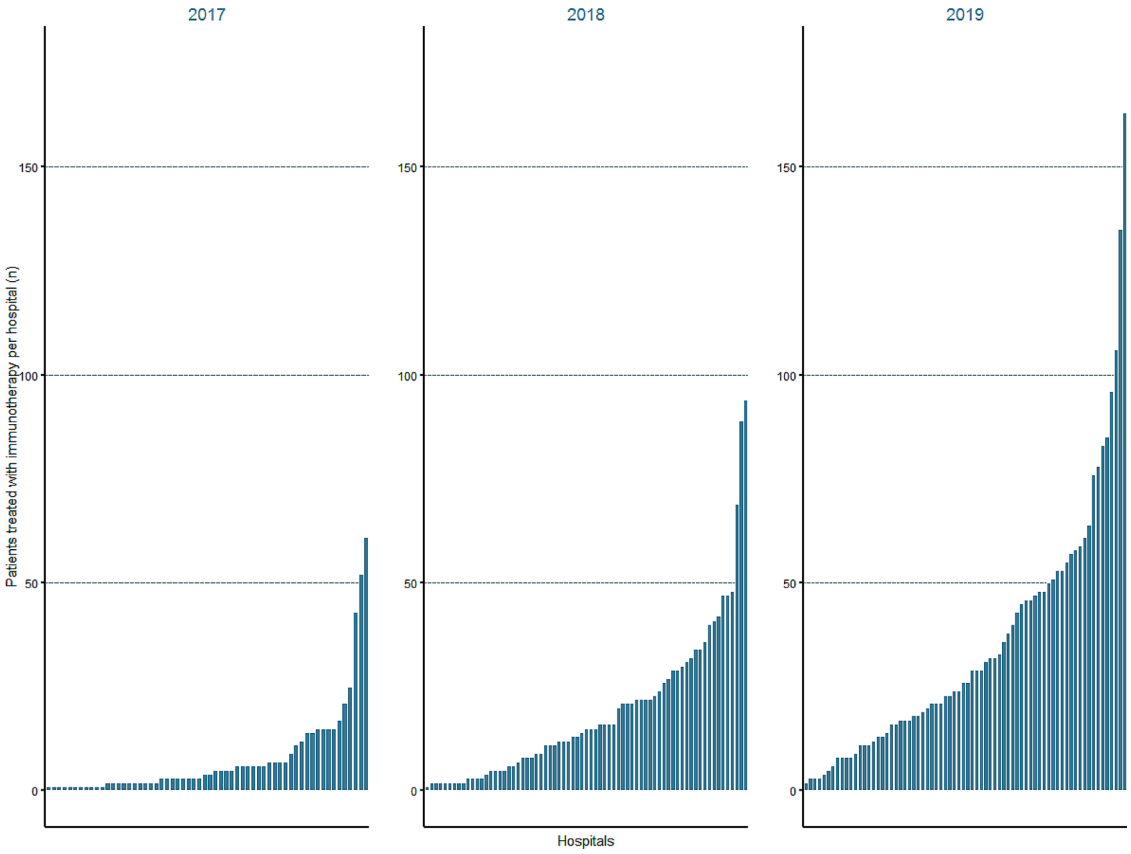

Fig. 3. Number of patients treated with immunotherapy per hospital from 2017 to 2019 in the Netherlands.

The NVALT registration showed that the use of nivolumab in the Netherlands was according to the trial inclusion criteria and that the real-world outcomes were similar to the studies [12]. In the years after, a broader patient population was treated with nivolumab. These data from the DLCA-L will be used to investigate differences in real-world and study patients and the impact on clinical outcomes. This evidence will be important for the efficient use of expensive treatments.

Real-world data outcomes from registries can also be used by regulators and health technology assessment organizations. Post-approval registry data could be used to gain information on real-world (long-term) safety and effectiveness. Furthermore, detailed information on molecular analyses, mutational burden, and outcomes of specific patient populations, excluded from phase-III trials can lead to improved insights in real-world effectiveness of medicines. These data are presently collected in the DLCA-L.

4.3. Limitations

A limitation of the present study and the first outcomes of the DLCA-L is that patients were registered as new patients when they are referred to other hospitals. Due to privacy regulations, the unique citizen service number of each individual cannot be shared with external parties other than the hospital. Therefore, the number of lung cancer patients can be overestimated. However, this does not affect the quality indicators since data of individual hospitals are shown for a specific part of the therapy or diagnosis. Double registration of patients affects the total number of patients, but it does not affect the number of patients treated with immunotherapy. Additional analyses of double registered patients showed <5% of the patients are registered more than once in the DLCA-L. This number is relatively low since all hospitals in the Netherlands, including peripheral hospitals, treat lung cancer. Patients are referred in case of second opinions, second primary tumors, or for immunotherapy (trial) treatments in specialized centers.

A second limitation of quality registries, in general, is the administrative registration burden associated with (manual) data collection. The database of the DLCA-L is extensive and very detailed since multiple aspects of lung cancer care are involved. Detailed information is necessary to correct (hospital) outcomes for case-mix. Future registration burden will be minimalized by automatic data retrieval and source linkage.

The third limitation of the DLCA-L might be the accuracy of the data. Real-world data are used, including patients treated in an uncontrolled setting. Examples of possible registration bias are reported ECOG PS or progression, which may be subjective in real-world practice. In clinical trials, more standardized and uniform criteria may have been used. Data registered in the DLCA-L derives from electronic patient files, which could include missing data or registered data, could be incorrectly be interpreted and registered. Therefore, multiple measures are taken to improve the data quality, such as the internal (by medical specialists) and external (by independent reviewers) data verification, the use of mandatory variables, and the use of validations and errors in the web-based registry. Data managers have been trained over the years. Interpretation mistakes are reduced with the use of manual and direct contact with the clinical audit managers. The percentage of complete cases is over 95 % with limited missing data in key variables in the dataset.

4.4. Future perspectives

Automated data retrieval from other data sources into the registry will be accomplished, leading to a reduced registration burden. The linkage of multiple existing data sources, such as administrative data of hospital pharmacies on expensive medicines, mortality information from national insurances, and filled electronic patient records in hospitals, will lead to more extensive and accurate information. National

insurance information on the date of death of patients will also reduce the need for long follow-up times of patients and, therefore, reduce the registration burden. The linkage of the sub-registries of the DLCA will also be valuable in the future, to receive insights into the complete lung cancer care of patients.

With increased treatment options and improved survival of stage IV NSCLC patients, quality of life becomes more important. Data collection on patient-reported outcomes measures (PROMs) can improve well-informed patient choices and shared decision making. Other DICA registries already have linked information of PROMs to the clinical data of the registry. Patients are requested to fill in the PROMs in a web-based environment at multiple time points in the treatment. This linkage could also be possible for the DLCA-L, using the questionnaires chosen by the International Consortium for Healthcare Outcomes Measurement (ICHOM) [29]. Individual participating hospitals are already using PROMs in daily clinical care, but these data are not yet linked to the clinical data from the DLCA-L. Other lung cancer registries, such as the Danish and Swedish, have included PROMs to measure the quality of life [3,24].

The measures taken to improve data quality stimulate the initiation of outcome quality indicators. The current indicators are mainly process- and structure indicators, but with the improving data quality, outcome indicators such as 1-year survival will be established. Outcome information is displayed in dynamic dashboards with filter options on patient-, tumor-, and treatment characteristics. Hospitals can get insights into specific patient populations and the treatments used in the hospital versus the benchmark (all other hospitals in the Netherlands). These dashboards also provide information on outcome trends, which makes it possible to visualize improvements over time.

Since the initiation of the DLCA-L in 2015, the registry has become a valuable and complete data source with national coverage in 2020. A high number of registered patients and limited missing data resulted in better insights into hospital processes and outcomes of lung cancer care. Quality indicators were, with success, used to establish improvements and minimize hospital variation. The DLCA-L also provides hospitals real-world information on the use of (systemic) therapies. These data will eventually lead to improved insights into real-world practice and outcomes to further improve lung cancer care in the Netherlands.

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R.K. Ismail: Conceptualization, Methodology, Software, Formal analysis, Visualization, Validation, Writing - original draft, Writing - review & editing. **F.M.N.H. Schramel:** Investigation, Writing - original draft, Writing - review & editing, Resources. **M. van Dartel:** Writing - original draft, Writing - review & editing, Validation, Software. **D.L. Hilarius:** Supervision, Writing - original draft, Writing - review & editing, Resources. **A. de Boer:** Writing - original draft, Writing - review & editing. **M.W.J.M. Wouters:** Methodology, Conceptualization, Writing - original draft, Writing - review & editing, Supervision. **H.J.M. Smit:** Supervision, Methodology, Conceptualization, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Supplementary data

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